In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 17-071V

(To be published)

AMANDA SAMUELS,	*	Chief Special Master Corcoran
Petitioner,	*	Filed: May 1, 2020
v.	*	
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	Entitlement Decision; Multiple Sclerosis; Acute Disseminated Encephalomyelitis; Tetanus, Diphtheria, Acellular Pertussis vaccine; Clinically Isolated Syndrome
Respondent.	*	

Diane Stedelnikas, Maglio Christopher & Toale, P.A., Sarasota, FL, for Petitioner.

Catherine Stolar, U.S. Dep't of Justice, Washington, D.C., for Respondent.

DECISION[1]

On January 17, 2017, Amanda Samuels filed a Petition under the National Vaccine Injury Compensation Program (the "Vaccine Program"[2]), alleging that the Tetanus-Diphtheria-acellular-Pertussis ("Tdap") vaccine she received on April 23, 2014, caused her to suffer acute disseminated encephalomyelitis ("ADEM") that subsequently evolved into multiple sclerosis ("MS"). Pet. at 1 (ECF No. 1). A hearing in this matter was held on November 19, 2019.

[1] This Decision will be posted on the United States Court of Federal Claims' website in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 (2012). **This means the Decision will be available to anyone with access to the internet**. As provided by 42 U.S.C. § 300aa-12(d)(4)(B), however, the parties may object to the published Decision's inclusion of certain kinds of confidential information. Specifically, under Vaccine Rule 18(b), each party has fourteen (14) days within which to request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Otherwise, the entire Decision will be available to the public in its current form. *Id.*

[2] The Vaccine Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3755 (codified as amended at 42 U.S.C. §§ 300aa-10–34 (2012)) (hereinafter "Vaccine Act" or "the Act"). All subsequent references to sections of the Vaccine Act shall be to the pertinent subparagraph of 42 U.S.C. § 300aa.

Having had the opportunity to review all materials filed in this case and consider the testimony offered at hearing, I hereby deny an entitlement award in this case. As stated in more detail below, there is no dispute that Petitioner's proper overall diagnosis is MS, not ADEM. And she did not successfully establish that the Tdap vaccine could, or did, cause her MS—regardless of how its initial presentation is characterized.

I. Factual Background

Ms. Samuels received the Tdap vaccine in her right deltoid from her primary care physician on April 23, 2014, because her sister was expecting a baby. Ex. 1 at 1. Four days later, on April 27, 2014, Ms. Samuels called her doctor, reporting blurry vision in the right eye, dizziness and nausea, and stating that her symptoms began the prior Thursday to Friday (April 24-25, 2014—hence 24 to 48 hours post-vaccination). Ex. 5 at 113. She was referred to an ophthalmologist, who evaluated her on April 27, 2014. Ex. 4 at 6. She confirmed her symptoms began on April 24th (and also acknowledged some history of migraines), and after examination was diagnosed with "likely ocular migraine, episodes of increased blurry vision in the right eye, left frontal headache." *Id.* at 7.

Ms. Samuels subsequently went back to her primary care physician, who confirmed the ocular migraine diagnosis, and a brain MRI was ordered. Ex. 5 at 113–14. Her differential diagnosis now included migraines, demyelinating disease, Lyme disease, and vasculitis. *Id.* at 118, 370. Then, on May 1, 2014, she saw a neurologist, Dr. Scott Kaplan. The results from imaging also came back, showing two nonspecific signals in her brain's right lobe white matter. *Id.* at 370. Based on such test results and examination, Dr. Kaplan opined that Petitioner likely had bilateral internuclear ophthalmoplegia ("INO").[3] *Id.* at 122–23. He additionally noted that Petitioner had been vaccinated approximately one week before, timing consistent with her having experienced an autoimmune reaction—but also observed the possibility that (if corroborated by additional test results) she might have MS. *Id.* at 123. The records from this visit also set forth that Petitioner reported having recently experienced a fever, and that her entire family had been sick around the time she received the Tdap vaccine. *Id.* at 121.

Petitioner next saw a neuro-ophthalmologist, Dr. Richard Feit, on May 5, 2014, reporting bilateral blurred vision and headaches beginning approximately eleven days prior. *See generally* Ex. 5 at 129–33. In reaction to Petitioner's reported history and initial exam, Dr. Feit confirmed the INO diagnosis and indicated that he "very strongly suspect[ed]" she had experienced some kind of demyelinating disease process. Ex. 5 at 131. Ms. Samuels then underwent a lumbar puncture on May 9, 2014, and testing of her cerebrospinal fluid ("CSF") revealed the presence

[3] INO is the disruption of horizontal movement of the eye, usually due to a lesion in the medial longitudinal fasciculus. *Dorland's Illustrated Medical Dictionary* 1329 (33d ed. 2020) (hereinafter *Dorland's*).

of oligoclonal bands[4] (a well-known biomarker for MS). *Id.* at 137, 140. Dr. Kaplan started Ms. Samuels on a five-day course of IVIG,[5] suspecting a demyelinating event but not certain that she was experiencing MS. *Id.* at 140, 163. Petitioner had a follow-up MRI at a subsequent visit in June 2014 that revealed unremarkable results, and by this time her vision had returned to baseline. A diagnosis of MS could not be made because she had only experienced one event, but test results were suggestive of MS, and Ms. Samuels was diagnosed as having suffered a clinically isolated syndrome ("CIS"). *Id.* at 168–70.

Almost six months later, on December 11, 2014, Ms. Samuels saw neurologist Dr. Jacob Sloane at Beth Israel Deaconess Medical Center, for evaluation and management of her suspected MS. Since her prior visit she had experienced some dizziness, characterized as fogginess or change in vision, headaches and fatigue, and a "wobbly feeling" with her eyes, but she denied any other problems with strength and sensation. Ex. 3 at 11. Dr. Sloane was reluctant to diagnose her with MS, but allowed that her existing presentation was consistent with "clinically isolated syndrome." *Id.* at 3.

Ms. Samuels presented for follow up with Dr. Sloane on multiple visits in 2015, during which she reported no new symptoms and had unremarkable examinations. The same was true for the following year. After a November 2016 visit, however, Dr. Sloane (who again observed no new or worsening neurological symptoms) recounted that Petitioner's neurological symptoms had begun after receipt of the Tdap vaccine in April 2014, and also that her initial presentation (especially in light of her subsequent course) was in his view most consistent with an ADEM designation. Ex. 3 at 26.

Petitioner's treaters thereafter continued to monitor her as time passed, and she largely remained stable through 2017 and 2018. *See*, *e.g.*, Ex. 29 at 6 (November 2017 visit with Dr. Sloane). Petitioner's health took a turn for the worse, however, in February 2019, when she experienced a new episode of double vision with an accompanying foggy sensation. Supplemental Affidavit of Amanda Samuels, filed Oct. 8, 2019 (ECF No. 49-2) at 5; Ex. 38 at 3. She presented to Dr. Sloane for a follow-up visit on March 18, 2019, and initially it was suspected that Petitioner was experiencing a pseudo-flare. Ex. 40 at 1–3. However, an updated MRI revealed the presence of new enhancing lesions in multiple white matter areas. Ex. 37 at 6–8. Based on these recurrent symptoms plus the imaging evidence, treaters now embraced an MS diagnosis for Ms. Samuels, and she is currently being so treated. *See generally* Ex. 37. Dr. Sloane has, however, continued to

[4] Oligoclonal bands are distinct bands of immunoglobulins that, when detected in CSF but are absent from serum, reveal antibodies associated with MS and other central nervous system diseases. *Dorland's* at 197.

[5] The abbreviation "IVIG" stands for "intravenous immunoglobulin," and it describes a common treatment for patients with immune system dysfunction. *See* N. Davis, *Medical Abbreviations* 178 (15th ed. 2011).

maintain that Petitioner's MS presented as ADEM in association with her receipt of the Tdap vaccine. Ex. 42 at 17.

II. Testimony at Hearing

A. *Petitioner's Witnesses*

1. Amanda Samuels

Ms. Samuels, an elementary school music teacher, testified at hearing on her own behalf, expanding on the circumstances of her illness. Tr. at 4–31. She recalled receiving the Tdap vaccine in April 2014, noting that she believed she had received it before in her life. *Id.* at 6–7. She reported experiencing an immediate malaise reaction[6] that same day that made her want to go to sleep early, followed by blurred vision the very next morning that she noticed while driving to her mother's house. *Id.* at 8–9. The vision changes, which progressively worsened, were accompanied by migraine pain (a preexisting concern, albeit one she associated primarily with hormonal changes). *Id.* at 7, 9. She did not experience a post-vaccination fever, pain, or inflammation at the site of vaccination, however. *Id.* at 28.

Around this time (approximately one day post-vaccination), Ms. Samuels called her primary care provider about her symptoms, but was informed that it was likely just an optical migraine, and that she should take her existing migraine medication. Tr. at 9. However, by the third day post-vaccination (April 26, 2014), her symptoms (which now included balance and trouble walking, which she partially attributed to her underlying vision difficulties) had become severe enough to encourage her to take herself to an urgent care provider, at which time she was referred to Massachusetts Eye and Ear, but was again told that her symptoms were likely migraine-related. *Id.* at 10–11, 28. She thereafter went back to her primary care physician, who obtained the MRI scan that first suggested the existence of a neurologic problem that could be MS. *Id.* at 11.

Petitioner recounted the next treatment assistance she obtained. Tr. at 12–13. Dr. Kaplan was the first treater to inform her directly (after observing on examination lagging eye tracking) that her illness was more than a migraine. *Id.* at 12. She noted that she was telling treaters at this time that her change in condition had occurred after receipt of the Tdap vaccine, although she deemed their responses to this information "noncommittal." *Id.* at 13. Eventually, Dr. Kaplan was able to use steroids to assist Ms. Samuels with her vision, and she recalled that his diagnostic work-up resulted in him proposing that she had experienced CIS. *Id.* at 13–14. She also learned at this time that although her spinal tap revealed that she possessed the oligoclonal bands associated with

[6] Ms. Samuels also testified to having had a fainting reaction (along with arm numbness and a frozen feeling in her neck) after receipt of the human papillomavirus vaccine in her mid-20s but added that such symptoms subsided in less than one month. Tr. at 7–8. She subsequently discontinued receipt of further doses of that vaccine. *Id.* at 8.

MS, the fact that she had only experienced one clinical neurologic episode meant that an MS diagnosis was not yet appropriate. *Id.* She did not recall informing Dr. Kaplan that two weeks before her visit to him, her family had been sick, or that she had been suffering herself from a fever, although the record so indicates. *Id.* at 25–26; *but see* Ex. 5 at 121 ("[t]wo weeks ago, she had a fever and her whole family was sick and around the same time she also got an immunization Tdap.").

Ms. Samuels subsequently saw a second neurologist, Dr. Sloane, later that month. Tr. at 14–15. He agreed with the CIS diagnosis, proposing a "wait and watch" responsive course of action. *Id.* at 15. As a result, although Petitioner had one January 2015 check-up visit, along with a few others "to make sure that nothing worse was happening" (*Id.)*, she primarily had six-month follow-up visits, in May and November 2015 respectively. *Id.* at 15–16. Up until the latter visit, Ms. Samuels recalls, she was not experiencing any significant changes, but she felt particularly frustrated by the late fall of that year, since she was still experiencing sensitivity to light or other stimuli like heat, any of which could impact her vision. *Id.* at 16. She also continued to suspect the Tdap vaccine was responsible for her condition—and testified that when she mentioned it to Dr. Sloane, he expressed the belief that it was "what triggered my MS." *Id.* at 17, 24.[7]

Despite Ms. Samuels's ongoing concerns about her health, her treaters scheduled her for a 12-month follow-up visit for the end of 2016. Tr. at 18. During this time period, Petitioner "was starting to finally feel a little bit more myself." *Id.* She became pregnant and gave birth in 2017, and follow-up examinations (including another MRI) revealed no new lesions, although treaters warned Ms. Samuels of the risk of a flare after pregnancy. *Id.* at 19–20. By this time, Petitioner's overall progress convinced treaters to put her on a five-year watch and wait monitoring plan. *Id.* at 20. Thus, in 2018 Petitioner only saw Dr. Sloane for annual treatments. *Id.* Ms. Samuels did not testify to experiencing any new or worsened symptoms for that year.

By the beginning of 2019, however, Petitioner began experiencing hand numbness, along with a recurrence of vision problems and "constant migraines." Tr. at 21.[8] Through her primary care physician, she was referred to an ophthalmologist, but later went back to Dr. Sloane. At first, Dr. Sloane diagnosed Petitioner with experiencing a pseudo-flare associated with fatigue from her new motherhood responsibilities, but a subsequent MRI revealed the development of new lesions in her brain. *Id.* at 22. In reaction, Dr. Sloane now felt comfortable diagnosing Ms. Samuels with MS, and prescribed a corticosteroid treatment. *Id.* at 23. She acknowledged, however, that she has

[7] When cross-examined, Ms. Samuels was not sure if there was a difference between Dr. Sloane proposing that the Tdap vaccine "triggered" her MS versus caused it. Tr. at 27–28.

[8] Ms. Samuels suggested in her testimony that in fact she may have begun to experience some kind of symptomatic flare the fall of 2018, evidenced by a constant feeling of exhaustion and incontinence, but had rationalized it as relating to her status as a new mother. Tr. at 21.

since continued to receive other vaccines, in light of the risks she faces from her MS. *Id.* at 24. None of these vaccinations have produced an MS symptoms flare. *Id.* at 29.

2. Dr. Lawrence Steinman

Dr. Steinman, a neurologist and immunologist, testified at hearing and filed three expert reports. Tr. at 31–100; Report, dated Dec. 18, 2017, filed as Ex. 6 (ECF No. 23-1) ("First Steinman Rep."); Report, dated July 13, 2018, filed as Ex. 35 (ECF No. 32-3); Report, dated Oct. 5, 2019, filed as Ex. 43 (ECF No. 48-2). He opined that the Tdap vaccine Petitioner received caused an innate immune response that resulted in a CNS neurologic injury—first manifesting as ADEM, but later progressing to MS.

Dr. Steinman currently serves as a professor in the departments of neurology, pediatrics, and genetics at Stanford University. Steinman Curriculum Vitae, filed as Ex. 44 (ECF No. 48-3) ("Steinman CV") at 1. He obtained his bachelor's degree from Dartmouth College before earning his medical degree from Harvard University. *Id.* He then completed his internship and residency in surgery, pediatrics, and pediatric and adult neurology at Stanford University. *Id.* He then completed several fellowships in the area of immunology. *Id.* He is board certified in neurology, though much of his work in the field also involves immunological concepts and theories. *Id.* at 2; Tr. at 33. Specifically, Dr. Steinman has expertise in the study of CNS disorders such as ADEM and MS. Tr. at 33. He estimates that he has treated thousands of patients with MS throughout his career. *Id.* at 34. Dr. Steinman currently spends approximately thirty percent of his time in clinical practice seeing patients, with the remainder of his time being allocated to research—for which he has published hundreds of articles—and administrative tasks. *Id.* The patients he most frequently sees are "one-shot-only" referrals, however, and he does not provide subsequent care following an initial referral. *Id.* at 34–35.

Dr. Steinman began with a discussion of the Tdap vaccine. In addition to its bacterial antigen components, it contains alum, included as an adjuvant to enhance the immune response elicited by the vaccine. Tr. at 37, 39. The bacterial components of the vaccine are adulterated toxins, or "toxoids," designed to generate an adaptive immune response, but without also inflicting the poisonous effects of the bacteria, and thereby provide subsequent immunologic protection from the "natural organism" on a subsequent exposure. *Id.* at 38–39. Although young children are on a regular schedule to get a comparable vaccine (known as "DTaP" when administered to children), adults are recommended to receive Tdap boosters every ten years. *Id.* at 37.

The causation theory offered in this case relies on the initial innate response to vaccination attributable in part to the function of the vaccine's adjuvant. As Dr. Steinman explained, the inclusion of alum in the Tdap vaccine causes the activation of certain immune cells called "cytokines," and in particular IL-1β, the cytokine known to trigger "the quintessential immune reaction called a fever." First Steinman Rep. at 8; Tr. at 39–40. This same cytokine is known to be

elevated in cases of CNS disease like ADEM or MS, while treatments intended to reduce the cytokine's presence help to ameliorate the diseases. Tr. at 41. In his view, a similar mechanistic immunologic process could explain either illness (although MS is unquestionably chronic in character). *Id.* at 57. Accordingly, the core contention of Dr. Steinman's theory was that the alum adjuvant prompted a pathologic immune system activation, resulting in neurologic harm presenting as ADEM but eventually leading to MS. *Id.* at 41.[9]

Dr. Steinman moved on to a review of the CNS diseases at issue in this case. MS, he explained, was named approximately 160 years ago. Tr. at 41. It involves neurologic inflammatory harm in more than one location of the brain or spinal cord, and tends to be chronic, with "relapses and remissions." *Id.* at 42, 52. It usually includes symptoms impacting vision, eye and motor movements, bladder or bowel control, and even cognition. *Id.* at 43. These kinds of symptoms (determined by exam or history), along with imaging and tests of the CSF (particularly for evidence of oligoclonal bands), help to diagnose MS. *Id.* at 43–44.[10] Most MS patients experience symptom relapses over time (termed "secondary progressive," or "relapsing-remitting"), although a less common form (primary progressive) simply worsens progressively. *Id.* at 52. Dr. Steinman considers Petitioner's MS to be the relapsing-remitting type. *Id.*

Dr. Steinman acknowledged that unlike other autoimmune-mediated diseases, such as lupus or neuromyelitis optica, the fact that a person has MS does not necessarily mean that he or she also possesses an aberrant immune system. Tr. at 77–78. As he put it, "other than the fact that their brains get attacked, generally [their immune system] behaves pretty normally." *Id.* at 77; *see also* Tr. at 79 ("you don't get [Guillain-Barré syndrome ("GBS")] after you develop MS"). Nevertheless, MS patients are treated with immunosuppressants—both because they impact the role the immune system plays in symptoms flare and disease progression, and also because scientific limits in understanding MS have prevented discovery of effective alternative therapies. *Id.* at 78–79.

[9] Dr. Steinman denied that the causation theory he was espousing was equivalent to the theory "autoimmune/inflammatory syndrome induced by adjuvants," or ASIA, despite his reliance on the alum component of the Tdap vaccine as perpetrating the disease, rather than the vaccine's bacterial toxoid components. Tr. at 96. ASIA has been questioned in the Vaccine Program as wholly lacking in reliable scientific support. *See, e.g.*, *Yalacki v. Sec'y of Health & Human Servs.*, No. 14-278V, 2019 WL 1061429, at *24 n.30 (Fed. Cl. Spec. Mstr. Jan. 31, 2019), *mot. for review den'd*, 146 Fed. Cl. 80 (2019) (noting several prior decisions in which special masters rejected the ASIA theory as scientifically unreliable).

[10] Dr. Steinman provided an extended discussion of some of the specific criteria used to diagnose MS, and the issues with why Petitioner was not immediately so diagnosed. Tr. at 44–46. But he agreed that Ms. Samuels ultimately *did* have MS. *Id.* at 45.

Because the "first" attack does not by itself establish MS's usual chronicity, it is often referred to as CIS[11]—the term some of Petitioner's treaters used to characterize her immediate post-vaccination symptoms. *Id.* Dr. Steinman, however, proposed that it was very difficult to distinguish ADEM from CIS at first glance, before it was known for a specific patient that the incident actually reflected his or her initial presentation of MS. Tr. at 42–43, 48. Thus, although he considered CIS to properly describe the first instance of an MS attack (*Id.* at 47), he termed it a "broad descriptor," and proposed that (consistent with the view that CNS inflammatory disorders exist on a continuum) it could include other diagnoses, such as ADEM. *Id.* at 48, 50.

Dr. Steinman characterized ADEM as a "first cousin" or "half-brother" of CIS, an acute condition featuring "disseminated inflammation in the brain." Tr. at 48. ADEM often features multiple brain lesions, making MRI imaging useful for diagnosis. *Id.* Encephalopathy or encephalitis is not required for the diagnosis, however, nor are there specific biomarkers that would help distinguish CIS from ADEM. *Id.* at 49. Dr. Steinman therefore maintained that it mattered little *how* Ms. Samuels's initial presentation was defined, since it clearly later progressed into MS. *Id*. at 51, 56. Dr. Sloane simply treated Petitioner as she presented over time, without concern for his prior diagnostic determinations. *Id.*

There is, Dr. Steinman contended, reliable scientific support for associating the Tdap vaccine with certain CNS inflammatory disorders. Tr. at 46. One large-scale epidemiologic study, for example, observed a somewhat increased risk of ADEM in a five to twenty-eight-day window after receipt of Tdap—a risk that he felt was broadened given the sheer number of individuals who receive that vaccine. *Id.;* R. Baxter et al., *Acute Demyelinating Events Following Vaccines: A Case-Centered Analysis,* 63 Clinical Infectious Diseases, 1456–62 (2016), filed as Ex. 12 (ECF No. 19-6) ("Baxter"). Baxter evaluated instances of the occurrence of two acute demyelinating diseases, transverse myelitis ("TM") and ADEM, within a field of nearly sixty-four million vaccinations (including almost six million Tdap recipients) derived from data maintained by the Vaccine Safety Datalink. Baxter at 1457. Despite its Tdap findings, Baxter nevertheless concluded that for all other considered vaccines (a total of 30), the risk of *either* demyelinating CNS injury after vaccine was exceedingly low. *Id.* at 1456–57.

Although Baxter does find as Dr. Steinman represented, he acknowledged that the heightened incidence the study observed was lost if the interval considered was broadened to a range of two to forty-two days (the earlier side of which better captures Petitioner's experience, since she reported onset within a day or two of vaccination). Tr. at 47; Baxter at 1460. Indeed, Baxter itself noted "caveats" to its finding on Tdap—in particular, (a) that there were only *two* instances in total where post-Tdap ADEM was observed, out of the nearly six-million samples,

[11] By contrast, radiologic isolated syndrome, or "RIS," is used to explain circumstances where an individual displays evidence of brain or spine lesions on an MRI but has no outward clinical manifestations of neurologic disease. Tr. at 99.

and (b) that the two instances themselves were somewhat idiosyncratic when the specific facts of each were taken into account. Baxter at 1461.[12] Dr. Steinman further acknowledged that he did not recall if Baxter addressed MS as well as ADEM, and also agreed that if it did not consider the risk of post-vaccination MS, his opinion as to the article's value herein might change. Tr. at 80. In fact, Baxter's authors explicitly *excluded* MS patients pre- and post-vaccination from their studied population. Baxter at 1457.

Looking at the relevant medical history, Dr. Steinman opined that Ms. Samuels's own experiences confirmed his theory. He did not dispute Petitioner's ultimate MS diagnosis, but noted that before her first constellation of symptoms, she had never displayed anything that might appear to be CIS or ADEM. Tr. at 53, 70. She also had no family history for autoimmune disease. He found especially significant the fact that, post-vaccination, she was diagnosed with INO, a condition characterized by eye movement limitations due to a lesion specifically located in a single place on the brainstem. *Id.* at 54. Ms. Samuels's INO symptoms were, in Dr. Steinman's estimation, critical evidence supporting his causation theory. *Id.* at 73.

Dr. Steinman agreed, however, that INO was generally deemed a "red flag" suggesting the presence of MS, given its unmistakable clinical presentation. *Id.* at 75–76. He also admitted no knowledge of literature associating INO as a neurologic side-effect of the Tdap vaccine. *Id.* at 76. Additionally, the record establishes that Petitioner suffered from headaches in the past—and Dr. Steinman allowed that migraines might also explain this condition. *Id.* Her subsequent course—including a long remittance, followed by a relapse in 2019—was otherwise consistent with MS, and thus Petitioner's initial post-vaccination symptoms had to be associated with her later history. *Id.* at 57–58. Dr. Steinman also noted that Dr. Sloane concluded in November 2015 that the vaccine was likely causal. *Id*. at 66.

Dr. Steinman felt that Ms. Samuels's ADEM was the product of a "multifactorial" process, combining the environmental stimulus of vaccination with a likely genetic predisposition, as well as her unquestionable prior exposure to the Tdap components. Tr. at 68–69, 82, 86. But he acknowledged that he could only assume (drawing upon his own expertise in studying MS) that Petitioner was predisposed to MS, and could not identify which genes specifically she might possess that would be involved. *Id.* at 77. Such assertions also contradicted his earlier emphasis on the fact that Ms. Samuels never displayed a propensity toward autoimmunity before her first MS flare—a factual omission that detracted somewhat from the conclusion she was likely to develop MS or some similar autoimmune condition. Ultimately, however, he was comfortable relying on the Tdap vaccine alone as causal. *Id.* at 87.

[12] Specifically, one of the cases had received Tdap eleven days before onset, and the other had received it along with a number of other vaccines administered contemporaneously. Baxter at 1461. Baxter's authors also noted that what caused the increase incidence rate was the fact that two, rather than the predicted one, case had occurred. *Id.*

Dr. Steinman also agreed that in addition to the INO symptoms, Petitioner was determined close in time to her first symptoms, via imaging, to have existing brain lesions—and that they were of "indeterminate duration." Tr. at 83. He thus allowed for the possibility that the lesions had been present before Ms. Samuels received the Tdap vaccine, but downplayed the significance of this finding. *Id.* at 83 (saying that the lesions might not have been "clinically relevant," thus allowing the vaccine still be to causal of Petitioner's initial symptoms), 98–99.[13] Alternatively, the observed lesions could be explained by the vaccine—although Dr. Steinman did not specify how they would have come into existence, and ultimately maintained that he "didn't spend any time" in connection with the formulation of his opinion assessing the age of the lesions and the impact this would have on his theory. *Id.* at 83. He added that even though Petitioner's treaters had not seemed to view the lesions as significant in diagnosing her, he "would have jumped in there and called it MS and treated it," rather than ADEM or CIS. *Id.* at 84.

Dr. Steinman also opined that the timeframe for Petitioner's first MS-related symptoms was medically acceptable. He admitted that an onset within twenty-four hours, which he agreed the evidence supported, "requires the most explanation" of any causal component of Ms. Samuel's claim. Tr. at 60, 70. To do so, Dr. Steinman relied in part on the concept of immune memory, which posits that prior exposure to an infectious or toxic antigen in the past makes it likely that subsequent exposures will cause a faster immune response. *Id.* at 61; First Steinman Rep. at 11.

Prior exposure to tuberculosis or the vaccine used to combat it in Europe could, for example, cause a subsequent response to occur as soon as eight or twelve hours post-second exposure. Tr. at 61–62, 84 (referencing L. Fan et al., *Variation of Mycobacterium tuberculosis Antigen-Specific IFN-γ and IL-17 Responses in Healthy Tuberculin Skin Test (TST)-Positive Human Subjects*, 7 PLoS One 1, 1–6 (2012), filed as Ex. 24 (ECF No. 20-9); T. Kardjito & J.M. Grange, *Immunological and Clinical Features of Smear-Positive Pulmonary Tuberculosis in East Java*, 61 Tuberculosis 231, 236–37 (1980), filed as Ex. 25 (ECF No. 20-10); T. Serane & B. Kothendaraman, *Tuberculin Test Can be Read after 24 Hours in Adolescent Children*, 60 J. Tropical Pediatrics 157, 160 (2014), filed as Ex. 23 (ECF No. 20-8)). Dr. Steinman also referenced a seminal study on the onset for a peripheral neuropathy, GBS, which revealed onset for a studied group of individuals was as fast as one day, and that more individuals experienced such a short onset than experienced onset forty-two days post-vaccination. Tr. at 62; L. Schonberger et al., *Guillain-Barré Syndrome Following Vaccination in the National Influenza Program, United States, 1976-77,* 110 Am. J. Epidemiology 105–23 (1979), filed as Ex. 26 (ECF No. 21-1) ("Schonberger").

[13] In so testifying, Dr. Steinman acknowledged the existence of RIS, in which a patient is inadvertently found to possess brain lesions without outward clinical manifestations of neurologic injury. Tr. at 99. He agreed such a person could live a long time without symptoms or knowledge of the lesions. *Id.* at 99–100.

Here, Dr. Steinman noted, Ms. Samuels had previously received prior booster injections of the Tdap vaccine, likely giving her just that sort of immune memory. Tr. at 62–63. He also deemed significant the prior reaction to the HPV vaccine that Petitioner reported, noting that, like Tdap, this vaccine contains alum as an adjuvant. *Id.* at 63. By contrast, Dr. Steinman discounted the fact that subsequent vaccines did not also cause Petitioner to relapse, claiming that the immune-suppressive drugs she was taking as part of her MS treatment likely protected her from an aberrant immune response. *Id.* at 63.

On cross-examination, Dr. Steinman attempted to explain how what had first seemed to be ADEM (usually thought to be a one-time, monophasic disease) became the first symptom of MS. Tr. at 80. He claimed that effective treatment helped resolve Petitioner's ADEM, and that this was consistent with the monophasic nature of the illness. Tr. at 71–72 ("[t]hat's why it's called ADEM. It very rarely relapses, . . .because relapsing ADEM, why isn't that relapsing-remitting MS? It's just nomenclature"). When asked if in fact ADEM was better understood to constitute a distinct neurologic condition from MS, Dr. Steinman explained that his overall view was to lump them together, and that literature supported the conclusion that ADEM was related to MS. *Id.* at 72, 90–91. He also noted that ADEM could itself relapse (although the literature he cited for this proposition seemed to suggest that something initially viewed as ADEM, when followed by a symptom relapse, should in retrospect be seen as the first manifestation of MS). Tr. at 88–90; L. Krupp et al., *International Pediatric Multiple Sclerosis Study Group Criteria for Pediatric Multiple Sclerosis and Immune-Mediated Central Nervous System Demyelinating Disorders: Revisions to the 2007 Definitions*, 19 Multiple Sclerosis J. 1261, 1263 (2013), filed as Ex. C Tab 5 (ECF No. 29-5) ("Krupp"). He also agreed that despite the above, ADEM and CIS could *both* be isolated, one-time events. Tr. at 93–94.

Dr. Steinman was also asked how the Tdap vaccine could cause what initially appeared to be a one-time, acute event to evolve into a chronic condition like MS. Dr. Steinman asserted that the cytokine elevation occasioned by vaccination resulted in these immune cells going into the CNS, "and they don't necessarily go out," meaning future relapses became likely. Tr. at 72–73.[14] But when asked how long this production of cytokines would continue post-vaccination, he could not fully answer ("I don't think it's been studied that carefully" (*Id.* at 73)), but maintained that the alum adjuvant itself likely "does hang around for a long time," estimating it would take days or weeks to metabolize before decreasing. *Id.* at 73–74. He admitted, however, that even if all the above were accurate, other factors might trigger subsequent MS relapses—and that this topic was not actually addressed in the papers he cited to establish how the *first* flare/MS symptom would occur. *Id.* at 74.

[14] Dr. Steinman also asserted that certain immune cells like macrophages might also transport alum into the brain, where it could contribute to cytokine upregulation. Tr. at 74.

B. *Respondent's Expert – Dr. Jeffrey Gelfand*

Dr. Gelfand, a neurologist, testified for Respondent at hearing and also submitted two expert reports. Tr. at 102–54; Report, dated Mar. 30, 2018, filed as Ex. A (ECF No. 27-1) ("First Gelfand Rep."); Report, dated Sept. 20, 2019, filed as Ex. D (ECF No. 42-1) ("Second Gelfand Rep."). He opined that the medical record did not support the conclusion that Petitioner's MS was caused by the Tdap vaccine.

Dr. Gelfand is a board-certified neurologist currently employed as a professor of neurology at the University of California, San Francisco. Dr. Gelfand Curriculum Vitae, filed as Ex. F (ECF No. 45-1) ("Gelfand CV") at 1. He obtained his bachelor's degree from Princeton University before receiving his medical degree from Harvard University. *Id.* He then completed his internship and residency in neurology at the University of California, San Francisco. *Id.* He subsequently completed a fellowship in the subspecialty areas of MS and neuroimmunology. *Id.* Much of Dr. Gelfand's clinical practice is focused on MS, neuroimmunology, and autoimmune neurology. *Id.* at 3; Tr. at 102. He has experience treating patients throughout all stages of MS, as well as patients experiencing ADEM and autoimmune encephalopathies. Tr. at 106. Beyond clinical work, Dr. Gelfand also conducts research and has published numerous articles on these subject areas. Gelfand CV at 13–22.

Dr. Gelfand first discussed what he saw in Ms. Samuels's medical history. Like Dr. Steinman, he noted that Petitioner's initial visual symptoms presented within a day of her receipt of the Tdap vaccine. Tr. at 108. Those symptoms evolved into the bilateral INO diagnosis she received not long thereafter, and he agreed this was a proper diagnosis. *Id.*at 108, 110, 137. As Dr. Gelfand explained, INO involves injury to "a very specific pathway in the brainstem" associated with coordinated eye movement. *Id.* at 108–09. It manifests with symptoms of double/blurry vision and is in his view a "classic archetypal syndrome" for MS or other demyelinating diseases (although it can be the result of a brainstem stroke in older patients with vascular disease). *Id.* at 109. He also agreed with Dr. Steinman that Petitioner's initial symptoms constituted her "first attack of relapsing-remitting [MS]." *Id.* at 110.

An initial demyelinating CNS injury Dr. Gelfand opined, would properly be considered CIS until a second incident, and thus CIS was the best diagnostic classification under such circumstances (i.e., where MS was suspected but could not yet be formally diagnosed). Tr. at 116, 133–34. He felt there was some "clinical utility" in having essentially a placeholder diagnosis for an initial neurologic CNS injury that warranted follow-up, allowing revision to the diagnosis "based on the new totality of the evidence" if the patient experienced subsequent symptoms. *Id.* at 132, 134. The CIS designation also allowed for more precise treatment. The immunosuppressive therapies used for MS, he noted, posed risks, and were also not the best approaches for treating a one-time, acute, monophasic inflammatory/demyelinating event. *Id.* He added that certain CIS

presentations might be corroborated with enough additional evidence suggestive of MS (whether MRI or CSF findings) to allow for MS-oriented treatments earlier on. *Id.* at 133.

Unlike Dr. Steinman, Dr. Gelfand believed there were features that distinguish ADEM from CIS, even if both were CNS-demyelinating afflictions. ADEM, he maintained, was medically understood to be "multifocal," meaning it did not target a single place in the body, most commonly affected children, and was otherwise a monophasic occurrence "that typically has a component of encephalopathy." Tr. at 116, 118–19. ADEM as a medical descriptor could not be interchangeably used to describe other common initial MS presenting symptoms, like optic neuritis. *Id.* at 117, 143 ("[i]f ADEM refers to a distinct pathophysiologic entity that's monophasic and multifocal and has a particular phenotype, that is a different entity than what we see as the typical MS disease process"). Although Dr. Gelfand agreed that a person might phenotypically appear to have ADEM but then go on to experience a neurologic relapse (and therefore need to be diagnostically reclassified as suffering from MS), in "the vast majority of cases" ADEM was an acute, "one-time event." *Id.* at 117. He therefore stressed the importance of maintaining a diagnostic distinction between CIS and ADEM. *Id.* at 135.

Under the facts of this case, Dr. Gelfand maintained that CIS and not ADEM best explained Petitioner's initial presentation. Tr. at 139–40. Only a very broad definition of ADEM, making it "synonymous with CIS," could properly explain a first MS symptoms presentation, but he insisted that CIS was more precise and overall, in his view, accurate. *Id.* at 144; Second Gelfand Rep. at 3 ("[t]he phenotype of a single episode of a single focus of inflammatory demyelination in the brainstem causing [INO] without evidence of injury to other areas of the nervous system and without encephalopathy supports a diagnosis of CIS and not what is generally considered under the ADEM diagnostic umbrella.").

In support, Dr. Gelfand referenced the "McDonald criteria" for diagnosing MS also referenced by Dr. Steinman. Tr. at 118, A. Thompson et al., *Diagnosis of Multiple Sclerosis: 2017 Revisions of the McDonald Criteria*, 17 Lancet Neurology 162, 162–73 (2018), filed as Ex. C Tab 4 (ECF No. 29-4) ("McDonald"). While INO (which the experts agree Ms. Samuels first experienced) is included as a kind of "focal brainstem syndrome," and therefore a common MS presenting symptom, an encephalopathic reaction like ADEM was at best *atypical* of MS. Tr. at 118 (referencing McDonald at 163). Dr. Gelfand agreed that even under the McDonald Criteria, individuals properly diagnosed as having initially experienced ADEM could also go on to experience MS (in which case ADEM would be the presenting symptom). Tr. at 135–36.[15] But despite the fact that ADEM and CIS have overlapping diagnostic features and Dr. Sloane's reliance

[15] Dr. Gelfand was less willing to accept that ADEM could be used as a diagnostic descriptor for a *second* MS flare/relapse. Tr. at 139.

on ADEM to explain Petitioner's presentation, Dr. Gelfand opined that CIS was the best diagnostic classification for Petitioner's initial post-vaccination symptoms. *Id.* at 137–38.

Next, Dr. Gelfand provided some context about the nature of MS and what is known about its possible causes or symptom triggers. MS "leads to a proinflammatory or misdirected immune system against the [CNS]." Tr. at 111. It is understood to be a chronic, non-monophasic condition, in which an ongoing inflammatory state causes different injuries (brain and spinal cord lesions and/or neurodegeneration). *Id.* at 111–12. He noted its causes were largely not understood by medical science, but that MS was accepted as an autoimmune disease with "multifactorial" elements behind it. *Id*. at 110. Genetics were accepted as a risk factor, and also some specific environmental factors (such as certain wild virus infections like Epstein-Barr, smoking, and even an individual's vitamin D levels or sunlight exposure). *Id.* at 111. In Dr. Gelfand's experience clinically, it was rare to ever successfully identify what had specifically instigated an individual's MS. *Id.*

Dr. Gelfand specifically questioned the reliability of Dr. Steinman's causal theory that cytokine upregulation could cause MS. He agreed that certain cytokines identified by Dr. Steinman, like IL-1β, were markers for the "active inflammatory process" that would characterize an existing case of MS. Tr. at 112; S. Hauser et al., *Cytokine Accumulation in CSF of Multiple Sclerosis Patients: Frequent Detection of Interleukin-1 and Tumor Necrosis Factor but not Interleukin-6,* 40 Neurology 1735–39 (1990), filed as Ex. 45 (ECF No. 48-4) ("Hauser"). But he disputed that the presence of those cytokines established their *causal* role in the MS process, or that they were specific to any particular disease. Tr. at 112–13. Hauser itself did not find the cytokines were causal. Hauser at 1737 (noting at best that some proinflammatory cytokines might either "participate" in lesion development or contribute to common MS symptoms felt during the disease, like fatigue). He also noted that the nature of MS did not line up well with what is known about cytokine propagation, post-vaccine or otherwise. The inflammation associated with MS is not "time-restricted to the acute attack" of the first MS presentation or any subsequent relapses, but is instead ongoing (as evidenced by CSF testing during a patient's course, which will continue to reveal the presence of oligoclonal bands—and thus that an active inflammatory response is present). *Id.* at 113.

There is no scientific explanation, Dr. Gelfand contended, for how a single vaccination could cause such an ongoing inflammatory milieu. Tr. at 114. Because cytokines do not have a long half-life, it could not be assumed that they would simply linger after their creation, but instead would have to be continuously replenished. *Id.* In addition, what medical science does know about MS suggests that the chronic inflammation it features is limited to/occurs *within* the CNS. *Id.* at 114–15 ("the theory is that there's an inflammatory process that takes hold and that even within the [CNS], there can be persistent chronic inflammation"). The chronicity of inflammation in MS

distinguishes it from acute and monophasic processes which may also involve CNS damage (and therefore may resemble an MS relapse). *Id.* at 115.

Besides expressing his views on MS generally and Ms. Samuels's presentation specifically, Dr. Gelfand addressed whether Tdap or any vaccine might be causal in this case. He disputed the existence of any scientific or medical literature associating the Tdap vaccine to Ms. Samuels's INO. Tr. at 119. He maintained that more broadly, vaccination was not deemed a risk factor in causing MS, citing a recent review article that considered other possible environmental triggers but did not include vaccines in its review. Tr. at 120, D. Reich et al., *Multiple Sclerosis,* 378 N. Eng. J. Med., 169–80 (2018), filed as Ex. G Tab 2 (ECF No. 46-2) ("Reich"). Reich noted risk factors such as gender (women more commonly experience MS) and geographic location (possibly associated with sunlight amounts in northern climes where MS is more prevalent), and listed environmental triggers like tobacco exposure, obesity, or prior exposure to the Epstein-Barr virus. Reich at 172–73. And even for such identified factors, "the mechanisms by which genetic polymorphisms and environmental exposures raise the risk of multiple sclerosis remain the subject of intense investigation." *Id.* at 173.[16]

Dr. Gelfand also referenced an epidemiologic study that specifically considered whether there was an association between MS and vaccination. A. Langer-Gould et al., *Vaccines and the Risk of Multiple Sclerosis and Other Central Nervous System Demyelinating Diseases,* 71 JAMA Neurology, 12:1506-13 (2014), filed as Ex. C Tab 8 (ECF No. 29-8) ("Langer-Gould"). Langer-Gould, a case-control study, specifically analyzed incident events of MS, CIS, and ADEM separately, comparing 780 incident cases of CNS injuries versus 3885 controls, but found no increased risk of ADEM or CIS in people less than age fifty with respect to all vaccines (including Tdap, which accounted for a large proportion of total vaccine exposures). Langer-Gould at 1511–12; First Gelfand Rep. at 12–13.

Other articles reached the same conclusions. Second Gelfand Rep. at 5 (citing M. Mailand & J. Frederiksen, *Vaccines and Multiple Sclerosis: A Systemic Review*, J. Neurology 1, 1–17 (2017), filed as Ex. G Tab 3 (ECF No. 46-3) ("Mailand"). A 2017 Systematic Review on vaccinations and MS risk published in the Journal of Neurology concluded that there was no evidence of increased risk of MS following tetanus, diphtheria, or pertussis vaccination, and the 2012 Institute of Medicine report concluded that the evidence was inadequate to accept or reject a causal relationship between diphtheria-toxoid, tetanus toxoid, or acellular pertussis containing vaccine and onset of MS in adults. Mailand at 2; Institute of Medicine, *Diphtheria Toxoid-,*

[16] Reich also suggests (contrary to the degree Petitioner's theory relies on a sudden innate immune response in the aftermath of vaccination as having triggered Petitioner's MS) that it is the *adaptive* arm of the immune response that plays a "critical" role in MS's pathogenesis. Reich at 173.

Tetanus Toxoid-, and Acellular Pertussis-Containing Vaccines, Adverse Effects of Vaccines, 525, 553 (2012).

Taking the above into account, Dr. Gelfand noted that in his clinical practice he recommends MS patients receive routine vaccines to ward off infections that (due to immunosuppressive treatments they receive) could be especially harmful—and even likely to *cause* MS flares themselves. Tr. at 120–22. He did admit, however, that there was evidence that certain vaccines could be causal of or contribute to *other* demyelinating conditions. *Id.* at 131.

In addition, Dr. Gelfand challenged Dr. Steinman's theory that Petitioner's short onset was reflective of an immune memory recall response. He particularly disputed that such a response would be "specific for the [CNS]," such that it would generate CNS-oriented inflammation sufficient to produce the kind of chronic disease process that characterizes MS. Tr. at 123. He agreed that some of Dr. Steinman's arguments about the speed of tuberculin response after re-exposure was reliable evidence of recall as a general matter, but denied that the same kind of recall process could reliably explain how a subsequent exposure to Tdap components, or merely its adjuvant, would result in a targeted CNS attack. *Id.* at 129.

Dr. Gelfand also addressed some of the literature referenced by Petitioner in support of timing and vaccine association generally. Schonberger, for example, involved GBS—a wholly different neuropathic injury that was known to be monophasic and acute, and therefore shed little light on the timing of MS's pathogenesis. *Id.* at 123–24. And although he agreed that Baxter did observe some statistically-significant association between Tdap and ADEM, that article specifically *excluded* from consideration individuals who experienced MS, either before or after vaccination. *Id.* at 125–26, 140–41; Baxter at 1457. During cross examination, Dr. Gelfand did not dispute that epidemiologic studies had to be structured so that they could detect rare events, but he denied that studies could not be aimed at determining the likelihood of MS after vaccination simply because the injury alleged was rare. Tr. at 141–42. In so maintaining, he noted that MS was more common than ADEM or TM (yet Baxter had looked at both), and that existing literature that he deemed reliable had not found an association between MS and the Tdap vaccine. *Id.* at 142.

At bottom, the only association between the Tdap vaccine Petitioner received and onset of her MS was temporal in nature. Tr. at 126. But Dr. Gelfand proposed that a sudden onset of a first MS flare might only suggest that the disease process had *preexisted* vaccination, progressing in a subclinical manner over time. *Id.* at 127. He specifically pointed to the fact that the lesions observed from the initial MRIs performed on Ms. Samuels were "clinically silent," in that they were distinguishable from the brainstem injury reflected in her INO symptoms. *Id.* at 130. Had these lesions only arisen post-vaccination, they should have been enhancing on imaging (which would reveal their active/recent character) but were not—and in fact may have preceded her vaccination for this reason, although he could not date them. *Id.* at 130, 153–54. He agreed,

however, that Petitioner's treaters had properly classified the lesions as nonspecific, and therefore he could not opine with certainty that they were part of her overall MS disease process, at least based on strict diagnostic criteria. *Id.* at 130, 149. The presence of these lesions at the time of Petitioner's first symptoms was suggestive of a longer-term problem, especially given what is now known about her overall course, but Dr. Gelfand agreed that her treaters were properly cautious in not overstating the significance of such findings (although Dr. Sloane nevertheless proposed a "watch and wait" approach based on all the findings together). *Id.* at 150–51.

Dr. Gelfand could not identify what might have caused Ms. Samuels's MS. Tr. at 147. He stressed his overall view that such matters remained generally scientifically unknown, and at best it is believed that MS has multifactorial origins. *Id.* He thus deemed the circumstances of the cause of Petitioner's illness not much different from what causes MS for most individuals. *Id.*

III. Procedural History

As noted above, this case was filed in January 2017. After the gathering and filing of medical records was completed, Respondent submitted his Rule 4(c) Report in August of that same year contesting the appropriateness of compensation. ECF No. 14. The parties then began the process of filing expert reports, starting with Dr. Steinman's first report in December 2017, and ending with a "second supplemental" report from Dr. Steinman in October 2019. In the interim time period, I set the matter for hearing to be held in November 2019, and the parties offered their prehearing filings in advance of that hearing. The hearing proceeded as scheduled, and the parties declined the opportunity to file post-hearing briefs, making the case now fully ripe for resolution.

IV. Applicable Legal Standards

A. *Petitioner's Overall Burden in Vaccine Program Cases*

To receive compensation in the Vaccine Program, a petitioner must prove either: (1) that he suffered a "Table Injury"—i.e., an injury falling within the Vaccine Injury Table—corresponding to one of the vaccinations in question within a statutorily prescribed period of time or, in the alternative, (2) that his illnesses were actually caused by a vaccine (a "Non-Table Injury"). *See* Sections 13(a)(1)(A), 11(c)(1), and 14(a), as amended by 42 C.F.R. § 100.3; § 11(c)(1)(C)(ii)(I); *see also Moberly v. Sec'y of Health & Human Servs.*, 592 F.3d 1315, 1321 (Fed. Cir. 2010); *Capizzano v. Sec'y of Health & Human Servs.*, 440 F.3d 1317, 1320 (Fed. Cir. 2006).[17] In this case, Petitioner does not assert a Table claim.

[17] Decisions of special masters (some of which I reference in this ruling) constitute persuasive but not binding authority. *Hanlon v. Sec'y of Health & Human Servs.*, 40 Fed. Cl. 625, 630 (1998). By contrast, Federal Circuit rulings concerning legal issues are binding on special masters. *Guillory v. Sec'y of Health & Human Servs.*, 59 Fed. Cl. 121,

For both Table and Non-Table claims, Vaccine Program petitioners bear a "preponderance of the evidence" burden of proof. Section 13(1)(a). That is, a petitioner must offer evidence that leads the "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [he] may find in favor of the party who has the burden to persuade the judge of the fact's existence." *Moberly*, 592 F.3d at 1322 n.2; *see also Snowbank Enter. v. United States*, 6 Cl. Ct. 476, 486 (1984) (mere conjecture or speculation is insufficient under a preponderance standard). Proof of medical certainty is not required. *Bunting v. Sec'y of Health & Human Servs.*, 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, a petitioner must demonstrate that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly*, 592 F.3d at 1321 (quoting *Shyface v. Sec'y of Health & Human Servs.*, 165 F.3d 1344, 1352–53 (Fed. Cir. 1999)); *Pafford v. Sec'y of Health & Human Servs*., 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner may not receive a Vaccine Program award based solely on his assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. Section 13(a)(1).

In attempting to establish entitlement to a Vaccine Program award of compensation for a Non-Table claim, a petitioner must satisfy all three of the elements established by the Federal Circuit in *Althen*: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of proximate temporal relationship between vaccination and injury." *Althen v. Sec'y of Health & Human Servs.*, 418 F.3d 1274, 1278 (Fed. Cir. 2005).

Each of the *Althen* prongs requires a different showing. Under *Althen* prong one, petitioners must provide a "reputable medical theory," demonstrating that the vaccine received *can cause* the type of injury alleged. *Pafford*, 451 F.3d at 1355–56 (citations omitted). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). Such a theory must only be "legally probable, not medically or scientifically certain." *Id.* at 549.

Petitioners may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health & Human Servs.*, 569 F.3d 1367, 1378–79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325–26). Special masters, despite their expertise, are not empowered by statute to conclusively resolve what are essentially thorny scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed "not through

124 (2003), *aff'd* 104 F. Appx. 712 (Fed. Cir. 2004); *see also Spooner v. Sec'y of Health & Human Servs.*, No. 13-159V, 2014 WL 504728, at *7 n.12 (Fed. Cl. Spec. Mstr. Jan. 16, 2014).

the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Id.* at 1380. Accordingly, special masters must take care not to increase the burden placed on petitioners in offering a scientific theory linking vaccine to injury. *Contreras v. Sec'y of Health & Human Servs.*, 121 Fed. Cl. 230, 245 (2015) ("[p]lausibility . . . in many cases *may* be enough to satisfy *Althen* prong one" (emphasis in original)).

In discussing the evidentiary standard applicable to the first *Althen* prong, many decisions of the Court of Federal Claims and Federal Circuit have emphasized that petitioners need only establish a causation theory's biological plausibility (and thus need not do so with preponderant proof). *Tarsell v. United States,* 133 Fed. Cl. 782, 792–93 (2017) (special master committed legal error by requiring petitioner to establish first *Althen* prong by preponderance; that standard applied only to second prong and petitioner's overall burden); *see also Contreras,* 121 Fed. Cl. at 245; *Andreu*, 569 F.3d at 1375. At the same time, there is contrary authority from the Federal Circuit suggesting that the same preponderance standard used overall in evaluating a claimant's success in a Vaccine Act claim is also applied specifically to the first *Althen* prong. *See, e.g.*, *Broekelschen v. Sec'y of Health & Human Servs.*, 618 F.3d 1339, 1350 (Fed. Cir. 2010) (affirming special master's determination that expert "had not provided a 'reliable medical or scientific explanation' *sufficient to prove by a preponderance of the evidence a medical theory* linking the [relevant vaccine to relevant injury]."") (emphasis added). Regardless, one thing remains: petitioners always have the ultimate burden of establishing their Vaccine Act claim *overall* with preponderant evidence. *W.C. v. Sec'y of Health & Human Servs.*, 704 F.3d 1352, 1356 (Fed. Cir. 2013) (citations omitted); *Tarsell*, 133 Fed. Cl. at 793 (noting that *Moberly* "addresses the petitioner's overall burden of proving causation-in-fact under the Vaccine Act" by a preponderance standard).

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375–77; *Capizzano*, 440 F.3d at 1326; *Grant v. Sec'y of Health & Human Servs.*, 956 F.2d 1144, 1148 (Fed. Cir. 1992). In establishing that a vaccine "did cause" injury, the opinions and views of the injured party's treating physicians are entitled to some weight. *Andreu*, 569 F.3d at 1367; *Capizzano*, 440 F.3d at 1326 ("medical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury'") (quoting *Althen*, 418 F.3d at 1280). Medical records are generally viewed as particularly trustworthy evidence, since they are created contemporaneously with the treatment of the patient. *Cucuras v. Sec'y of Health & Human Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993).

Medical records and statements of a treating physician, however, do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. Section 13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment,

test result, report, or summary shall not be binding on the special master or court"); *Snyder v. Sec'y of Health & Human Servs*., 88 Fed. Cl. 706, 746 n.67 (2009) ("there is nothing . . . that mandates that the testimony of a treating physician is sacrosanct—that it must be accepted in its entirety and cannot be rebutted"). As with expert testimony offered to establish a theory of causation, the opinions or diagnoses of treating physicians are only as trustworthy as the reasonableness of their suppositions or bases. The views of treating physicians should be weighed against other, contrary evidence also present in the record—including conflicting opinions among such individuals. *Hibbard v. Sec'y of Health & Human Servs.*, 100 Fed. Cl. 742, 749 (2011) (not arbitrary or capricious for special master to weigh competing treating physicians' conclusions against each other), *aff'd*, 698 F.3d 1355 (Fed. Cir. 2012); *Veryzer v. Sec'y of Dept. of Health & Human Servs.*, No. 06-522V, 2011 WL 1935813, at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), *mot. for review denied*, 100 Fed. Cl. 344, 356 (2011), *aff'd without opinion*, 475 F. Appx. 765 (Fed. Cir. 2012).

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Human Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must align with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id.* at 1352; *Shapiro v. Sec'y of Health & Human Servs.*, 101 Fed. Cl. 532, 542 (2011), *recons. denied after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem.*, 503 F. Appx. 952 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Human Servs.*, No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for rev. denied* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

B. *Legal Standards Governing Factual Determinations*

The process for making determinations in Vaccine Program cases regarding factual issues begins with consideration of the medical records. Section 11(c)(2). The special master is required to consider "all [] relevant medical and scientific evidence contained in the record," including "any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death," as well as the "results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions." Section 13(b)(1)(A). The special master is then required to weigh the evidence presented, including contemporaneous medical records and testimony. *See Burns v. Sec'y of Health & Human Servs*., 3 F.3d 415, 417 (Fed. Cir. 1993) (it is within the special master's discretion to determine whether to afford greater weight to contemporaneous medical records than to other evidence, such as oral testimony surrounding the

events in question that was given at a later date, provided that such determination is evidenced by a rational determination).

Medical records that are created contemporaneously with the events they describe are presumed to be accurate and "complete" (i.e., presenting all relevant information on a patient's health problems). *Cucuras*, 993 F.2d at 1528; *Doe/70 v. Sec'y of Health & Human Servs.*, 95 Fed. Cl. 598, 608 (2010) ("[g]iven the inconsistencies between petitioner's testimony and his contemporaneous medical records, the special master's decision to rely on petitioner's medical records was rational and consistent with applicable law"), *aff'd sub nom. Rickett v. Sec'y of Health & Human Servs*., 468 F. Appx. 952 (Fed. Cir. 2011) (non-precedential opinion). This presumption is based on the linked propositions that (i) sick people visit medical professionals; (ii) sick people honestly report their health problems to those professionals; and (iii) medical professionals record what they are told or observe when examining their patients in as accurate a manner as possible, so that they are aware of enough relevant facts to make appropriate treatment decisions. *Sanchez v. Sec'y of Health & Human Servs.*, No. 11-685V, 2013 WL 1880825, at *2 (Fed. Cl. Spec. Mstr. Apr. 10, 2013); *Cucuras v. Sec'y of Health & Human Servs.*, 26 Cl. Ct. 537, 543 (1992), *aff'd*, 993 F.2d at 1525 (Fed. Cir. 1993) ("[i]t strains reason to conclude that petitioners would fail to accurately report the onset of their daughter's symptoms").

Accordingly, if the medical records are clear, consistent, and complete, then they should be afforded substantial weight. *Lowrie v. Sec'y of Health & Human Servs.*, No. 03-1585V, 2005 WL 6117475, at *20 (Fed. Cl. Spec. Mstr. Dec. 12, 2005). Indeed, contemporaneous medical records are generally found to be deserving of greater evidentiary weight than oral testimony—especially where such testimony conflicts with the record evidence. *Cucuras*, 993 F.2d at 1528; *see also Murphy v. Sec'y of Dep't of Health & Human Servs.*, 23 Cl. Ct. 726, 733 (1991) (citing *United States v. United States Gypsum Co.*, 333 U.S. 364, 396 (1947) ("[i]t has generally been held that oral testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight.")).

There are, however, situations in which compelling oral testimony may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. *Campbell v. Sec'y of Health & Human Servs*., 69 Fed. Cl. 775, 779 (2006) ("like any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking"); *Lowrie*, 2005 WL 6117475, at *19 ("'[w]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent'") (quoting *Murphy*, 23 Cl. Ct. at 733)). Ultimately, a determination regarding a witness's credibility is needed when determining the weight that such testimony should be afforded. *Andreu*, 569 F.3d at 1379; *Bradley v. Sec'y of Health & Human Servs*., 991 F.2d 1570, 1575 (Fed. Cir. 1993).

When witness testimony is offered to overcome the presumption of accuracy afforded to contemporaneous medical records, such testimony must be "consistent, clear, cogent, and compelling." *Sanchez*, 2013 WL 1880825, at *3 (citing *Blutstein v. Sec'y of Health & Human Servs*., No. 90-2808V, 1998 WL 408611, at *5 (Fed. Cl. Spec. Mstr. June 30, 1998)). In determining the accuracy and completeness of medical records, the Court of Federal Claims has listed four possible explanations for inconsistencies between contemporaneously created medical records and later testimony: (1) a person's failure to recount to the medical professional everything that happened during the relevant time period; (2) the medical professional's failure to document everything reported to her or him; (3) a person's faulty recollection of the events when presenting testimony; or (4) a person's purposeful recounting of symptoms that did not exist. *Lalonde v. Sec'y of Health & Human Servs*., 110 Fed. Cl. 184, 203-04 (2013), *aff'd*, 746 F.3d 1334 (Fed. Cir. 2014). In making a determination regarding whether to afford greater weight to contemporaneous medical records or other evidence, such as testimony at hearing, there must be evidence that this decision was the result of a rational determination. *Burns*, 3 F.3d at 417.

C. *Analysis of Expert Testimony*

Establishing a sound and reliable medical theory often requires a petitioner to present expert testimony in support of his claim. *Lampe v. Sec'y of Health & Human Servs*., 219 F.3d 1357, 1361 (Fed. Cir. 2000). Vaccine Program expert testimony is usually evaluated according to the factors for analyzing scientific reliability set forth in *Daubert v. Merrell Dow Pharmaceuticals, Inc.*, 509 U.S. 579, 594–96 (1993). *See Cedillo v. Sec'y of Health & Human Servs.*, 617 F.3d 1328, 1339 (Fed. Cir. 2010) (citing *Terran v. Sec'y of Health & Human Servs.*, 195 F.3d 1302, 1316 (Fed. Cir. 1999)). "The *Daubert* factors for analyzing the reliability of testimony are: (1) whether a theory or technique can be (and has been) tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and (4) whether the theory or technique enjoys general acceptance within a relevant scientific community." *Terran*, 195 F.3d at 1316 n.2 (citing *Daubert*, 509 U.S. at 592–95).

The *Daubert* factors play a slightly different role in Vaccine Program cases than they do when applied in other federal judicial fora (such as the district courts). *Daubert* factors are usually employed by judges (in the performance of their evidentiary gatekeeper roles) to exclude evidence that is unreliable and/or could confuse a jury. In Vaccine Program cases, by contrast, these factors are used in the *weighing* of the reliability of scientific evidence proffered. *Davis v. Sec'y of Health & Human Servs*., 94 Fed. Cl. 53, 66–67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"). The flexible use of the *Daubert* factors to evaluate the

persuasiveness and reliability of expert testimony has routinely been upheld. *See, e.g.*, *Snyder*, 88 Fed. Cl. at 742–45. In this matter (as in numerous other Vaccine Program cases), *Daubert* has not been employed at the threshold, to determine what evidence should be admitted, but instead to determine whether expert testimony offered is reliable and/or persuasive.

Respondent frequently offers one or more experts of his own in order to rebut a petitioner's case. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen*, 618 F.3d at 1347 (citing *Lampe*, 219 F.3d at 1362). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)); *see also Isaac v. Sec'y of Health & Human Servs*., No. 08-601V, 2012 WL 3609993, at *17 (Fed. Cl. Spec. Mstr. July 30, 2012), *mot. for rev. denied*, 108 Fed. Cl. 743 (2013), *aff'd*, 540 F. Appx. 999 (Fed. Cir. 2013) (citing *Cedillo*, 617 F.3d at 1339). Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Moberly*, 592 F.3d at 1325–26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); *see also Porter v. Sec'y of Health & Human Servs*., 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("this court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act").

Expert opinions based on unsupported facts may be given relatively little weight. *See Dobrydnev v. Sec'y of Health & Human Servs.*, 556 F. Appx. 976, 992–93 (Fed. Cir. 2014) ("[a] doctor's conclusion is only as good as the facts upon which it is based") (citing *Brooke Group Ltd. v. Brown & Williamson Tobacco Corp.*, 509 U.S. 209, 242 (1993) ("[w]hen an expert assumes facts that are not supported by a preponderance of the evidence, a finder of fact may properly reject the expert's opinion")). Expert opinions that fail to address or are at odds with contemporaneous medical records may therefore be less persuasive than those which correspond to such records. *See Gerami v. Sec'y of Health & Human Servs.*, No. 12-442V, 2013 WL 5998109, at *4 (Fed. Cl. Spec. Mstr. Oct. 11, 2013), *aff'd*, 127 Fed. Cl. 299 (2014).

D. *Consideration of Medical Literature*

Both parties filed medical and scientific literature in this case, but not every filed item factors into the outcome of this decision. While I have reviewed all the medical literature submitted in this case, I discuss only those articles that are most relevant to my determination and/or are central to Petitioner's case—just as I have not exhaustively discussed every individual medical

record filed. *Moriarty v. Sec'y of Health & Human Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("[w]e generally presume that a special master considered the relevant record evidence even though he does not explicitly reference such evidence in his decision") (citation omitted); *see also Paterek v. Sec'y of Health & Human Servs.,* 527 F. Appx. 875, 884 (Fed. Cir. 2013) ("[f]inding certain information not relevant does not lead to—and likely undermines—the conclusion that it was not considered").

E. *Consideration of Comparable Special Master Decisions*

In reaching a decision in this case, I have considered other decisions issued by special masters (including my own) involving similar injuries, vaccines, or circumstances. I also reference some of those cases in this Decision, in an effort to establish common themes, as well as demonstrate how prior determinations impact my thinking on the present case.

There is no error in doing so. It is certainly correct that prior decision in different cases do not *control* the outcome herein.[18] *Boatmon v. Sec'y of Health & Human Servs.,* 941 F.3d 1351, 1358–59 (Fed. Cir. 2019); *Hanlon v. Sec'y of Health & Human Servs.*, 40 Fed. Cl. 625, 630 (1998). Thus, the fact that another special master reasonably determined elsewhere, on the basis of facts not in evidence in this case, that preponderant evidence supported the conclusion that vaccine X caused petitioner's injury Y does not compel me to reach the same conclusion in *this* case. Different actions present different background medical histories, different experts, and different items of medical literature, and therefore can reasonably result in contrary determinations.

However, it is *equally* the case that special masters reasonably draw upon their experience in resolving Vaccine Act claims. *Doe v. Sec'y of Health & Human Servs.,* 76 Fed. Cl. 328, 338–39 (2007) ("[o]ne reason that proceedings are more expeditious in the hands of special masters is that the special masters have the *expertise and experience to know the type of information that is most probative of a claim*") (emphasis added). They would therefore be remiss in ignoring prior cases presenting similar theories or factual circumstances, along with the reasoning employed in reaching such decisions. This is especially so given that special masters not only routinely hear from the same experts in comparable cases, but are also repeatedly offered the *same* items of medical literature regarding certain common causation theories. It defies reason and logic to obligate special masters to "reinvent the wheel", so to speak, in each new case before them, paying no heed at all to how their colleagues past and present have addressed similar causation theories

[18] By contrast, Federal Circuit rulings concerning legal issues are binding on special masters. *Guillory v. Sec'y of Health & Human Servs.*, 59 Fed. Cl. 121, 124 (2003), *aff'd* 104 F. Appx. 712 (Fed. Cir. 2004); *see also Spooner v. Sec'y of Health & Human Servs.*, No. 13-159V, 2014 WL 504728, at *7 n.12 (Fed. Cl. Spec. Mstr. Jan. 16, 2014). Special masters are also bound within a specific case by determinations made by judges of the Court of Federal Claims after a motion for review is resolved.

or fact patterns. It is for this reason that prior decisions can have high persuasive value—and why special masters often explain how a new determination relates to such past decisions.[19] Even if the Federal Circuit does not *require* special masters to distinguish other relevant cases (*Boatmon,* 941 F.3d at 1358), it is still *wise* to do so.

ANALYSIS

I. Overview of ADEM, MS, and Their Overlapping Features

On several prior occasions, I have considered the relationship between ADEM and MS in resolving a Vaccine Act claim. *See, e.g.*, *Taylor v. Sec'y of Health & Human Servs.*, No. 13-700V, 2018 WL 2050857, at *20–21 (Fed. Cl. Spec. Mstr. Mar. 9, 2018) (comparing the diagnoses of ADEM and MS). In short, reliable science supports the conclusion that ADEM is best understood as an acute and monophasic CNS demyelinating illness that does not recur. National Multiple Sclerosis Society, *Acute Disseminated Encephalomyelitis (ADEM)*, https://www.nationalmssociety.org/What-is-MS/Related-Conditions/Acute-Disseminated-Encephalomyelitis-(ADEM) (last visited Apr. 9, 2020), filed as Ex. 31 (ECF No. 30-4). Consistent with the testimony of Drs. Steinman and Gelfand, ADEM more often than not afflicts children, generally does not repeat, and often has encephalopathic features like fever, headache, confusion, vomiting, and seizures. *Id.*

Consistent with its sudden appearance and fast disease course, ADEM has been found to be an injury that can be vaccine-caused. *Brown v. Sec'y of Health & Human Servs.*, No. 09-426V, 2011 WL 5029865, at *45 (Fed. Cl. Spec. Mstr. Sept. 30, 2011); *Kuperus v. Sec'y of Health & Human Servs.*, No. 01-060V, 2003 WL 22912885, at *11 (Fed. Cl. Spec. Mstr. Oct. 23, 2003). The very immune-stimulating effects of different vaccines can theoretically cause a sudden autoimmune attack on CNS myelin, resulting in a demyelinating injury. *Brown*, 2011 WL 5029865, at *45.[20] However, not all such claimants have succeeded—especially when onset

[19] Consideration of prior determinations is a two-way street that does not only inure to the benefit of one party. Thus, I would likely take into account the numerous decisions finding no association between vaccination and autism when confronted with a new claim asserting autism as an injury and have informed such claimants early in the life of their case that the claim was not viable for just that reason. But I would *also* deem a non-Table claim asserting GBS after receipt of the flu vaccine as not requiring extensive proof on *Althen* prong one "can cause" matters, for the simple reason that the Program has repeatedly litigated the issue in favor of petitioners.

[20] Such successful cases also frequently rely, in large or small part, on what is known about how the immune system can play a role in causing *peripheral* nerve injuries, such as GBS. *See, e.g.*, *Stewart v. Sec'y of Health & Human Servs.*, No. 06-777, 2011 WL 3241585, at *16–18, 21 (Fed. Cl. Spec. Mstr. July 8, 2011) (discussing the scientific and medical theories for how vaccines can cause GBS).

appeared too sudden. *Orloski v. Sec'y of Health & Human Servs.,* No. 17-936V, 2019 WL 7565495, at *15 (Fed. Cl. Spec. Mstr. Oct. 31, 2019) (immediate onset of alleged Tdap/influenza vaccine-caused ADEM too short, in light of literature suggesting a median onset of two weeks for comparable demyelinating diseases).

MS, by contrast, is qualitatively different, despite the fact that it too involves CNS demyelinating injuries and is believed to be autoimmune in mechanism. MS is a chronic disease process that, regardless of its initial presentation, will recur and/or in severe cases progress. Krupp at 1263. In addition, MS can be subclinical and symptomatically silent for a long period of time, with MS-characteristic brain lesions often discovered in the absence of symptoms, or non-recent lesions discovered only after clinical manifestations. *See* McDonald at 163; Reich at 176. And significantly (and of course independent of the burden of proof petitioners bear in Program cases), there is little to no direct scientific knowledge as to *why* MS recurs—and no similar evidence that a one-time neurologic "hit" can produce subsequent symptoms months or years later. Tr. at 74; J. Gelfand, *Risk of Multiple Sclerosis After a Clinically Isolated Syndrome: From Magnetic Resonance Imaging to Oligoclonal Bands to Activated T Cells*, 74 JAMA Neurology 262, 262 (2017), filed as Ex. C Tab 3 (ECF No. 29-3).

Because of the above, special masters have denied compensation in cases alleging MS as a vaccine-caused injury despite the overlap between ADEM, TM, and MS. *See, e.g.*, *Hunt v. Sec'y of Health & Human Servs.*, No. 12-232V, 2015 WL 1263356, *15 (Fed. Cl. Spec. Mstr. Feb. 23, 2015) (denying entitlement where MS was the alleged injury, but the literature offered discussed causal relationship between vaccines and ADEM). Admittedly, some special masters have gone in the opposite direction, and granted compensation in MS cases—but my review of those decisions does not reveal any reasoned efforts to grapple with the distinctions explored above. *See, e.g.*, *Hitt v. Sec'y of Health & Human Servs.*, No. 15-1283V, 2020 WL 831822, at *9–10 (Fed. Cl. Spec. Mstr. Jan. 24, 2020). Rather, their assumption appears to have been that if a vaccine can cause one kind of CNS autoimmune demyelinating injury, it can cause another.

II. Petitioner Has Not Preponderantly Established the Tdap Vaccine Could or Did Injure Her

A. Petitioner's Initial Symptoms are Best Characterized as CIS Rather than ADEM

In many cases, the first step in deciding a claim is to determine the nature of the petitioner's injury—especially if the causal theory is dependent on establishing that a specific injury occurred. *Broekelschen*, 618 F.3d at 1345; *LaPierre v. Sec'y of Health & Human Servs.*, No. 17-227V, 2019 WL 6490730, at *16–17 (Fed. Cl. Spec. Mstr. Oct. 18, 2019). Here, the parties agree that Ms. Samuels suffers from MS, but that diagnostic determination could not be made until 2019—well

after the claim was filed. This placed Petitioner's overall post-vaccination symptoms in a new light, and forced her to recast her claim somewhat—from one arguing that her initial symptoms were an acute, one-time event (ADEM), to contending that her subsequent MS only *presented* as ADEM.

Overall, this is not a case where defining the injury is key to its resolution. Petitioner not only does not dispute her MS diagnosis, but alleges that the Tdap vaccine was *ultimately* responsible for her injuries, however her initial presentation is defined. But the parties nevertheless dispute the best diagnostic classification for Petitioner's *initial* symptoms, and their disagreement on this topic has some significance, since ADEM is often deemed a compensable vaccine injury. I find that the record and expert testimony best supports CIS, rather than ADEM, as the proper descriptor of Petitioner's presenting symptoms.

Dr. Gelfand persuasively established that there are meaningful clinical and diagnostic differences between ADEM and CIS. Even if ADEM is a type of CNS demyelinating injury, and even if it can constitute an initial MS "flare," from a medical/scientific standpoint it is *better* understood as a narrower condition in most cases than Dr. Steinman allowed, with symptoms specific to it that are distinguishable from a first MS presentation. Treatment implications also make CIS a better "placeholder" term for what might later become MS. Indeed, Petitioner's own medical history reveals that her treaters not only suspected MS right away and anticipated the possibility of an eventual MS diagnosis, but adopted a watch-and-wait approach with her over the four-plus years that transpired between flares. In addition, Ms. Samuels's presenting symptom of INO does appear to be common in MS, but was not shown by Petitioner to be as reasonably understood to be a feature of ADEM. Dr. Steinman's ADEM definition was otherwise too broad to be diagnostically meaningful.

It is correct that the medical history establishes that treaters like Dr. Sloane have characterized Petitioner's initial symptoms as ADEM, even in the face of the subsequent MS diagnosis. But (putting aside that I need not accept as sacrosanct any treater view) this does not alter the fact that however initially characterized, Petitioner's ultimate, correct diagnosis was *not* ADEM, at least as it is commonly understood as a monophasic and acute demyelinating injury—and thus Petitioner needed to preponderantly demonstrate that the Tdap vaccine was responsible for her overall disease course.[21] She did not (and I address the *Althen* prongs below, in order of their significance to my determination).

[21] I note that Petitioner did not advance the theory that her vaccine-caused injury was *only* ADEM, and that her subsequent MS was unrelated.

B. The *Althen* Prongs Have not Been Met in This Case

1. *Althen* Prong One

Petitioner was unable to preponderantly establish that the Tdap vaccine can cause MS. First, as discussed above, reliable scientific evidence does not support the conclusion that *any* vaccine is associated with MS, including Tdap. *See generally* Reich, Langer-Gould. Articles that seem to support a contrary view, like Baxter, do not consider MS at all, and even only *weakly* support the conclusion that the Tdap vaccine is associated with ADEM (which I do not otherwise find Petitioner had, at least in its most commonly-understood sense). Thus, what evidence that was offered regarding vaccines, and Tdap specifically, did not support Petitioner's causation theory.

Second, the mechanism Petitioner embraces—generalized inflammation promoted by an innate immune response to the Tdap vaccine's adjuvant, alum—is not scientifically/medically reliable. The literature filed by Petitioner, such as Hauser, at best establishes that cytokines are *present* or *involved* in an ongoing MS disease process—not that they instigate it, or can independently maintain it over a lengthy timeframe. There is far too little known about MS to conclude that the expected immune response to a vaccine could quickly inflict the kind of neurologic harm ultimately associated with MS well down the road. Here, the chronic nature of MS becomes especially important. Even if a vaccine's upregulation of cytokines could produce a one-time injury to the CNS, such as ADEM or TM, how this becomes chronic later was wholly unexplained by Petitioner. And the central role the Tdap adjuvant is alleged to play in all of the above was also not adequately elucidated. Indeed, despite Dr. Steinman's protestations to the contrary, the theory he embraced about the pathologic impact of an adjuvant is dangerously close to the discredited ASIA theory, which assumes that alum lingers in the body for long periods of time and causes subsequent harm simply due to its presence. *Yalacki*, 2019 WL 1061429, at *24 n.30.

Dr. Steinman's inconsistent treatment of ADEM herein illustrates the deficiencies in Petitioner' causation theory. On the one hand, he correctly noted that ADEM overlaps substantially with MS—both are autoimmune-mediated conditions that impact the CNS and have common initial presenting symptoms—as well as that MS can, in effect, be initially "mistaken" as ADEM (since MS can only be *suspected* as of the first evidence of symptoms—it cannot be *diagnosed* until a second flare or relapse occurs). But does this make ADEM and MS equivalent? No, by Dr. Steinman's admission, since ADEM is most commonly a one-time, non-recurring event. Tr. at 93–94. Indeed, the literature filed in this case better supports the conclusion that ADEM *should* be so-considered—*not* that ADEM is simply a term that can flexibly be applied to the first MS symptom, interchangeable with CIS.

Another important distinction between ADEM and MS that Dr. Steinman unsuccessfully elided is the temporal character of each. ADEM is generally acute and monophasic, while MS is chronic. As a result, the causation theory in this case needed to explain how an initial and quite-acute neurologic attack could initially be mediated by a vaccine, later becoming an ever-present risk for Petitioner that would manifest in a new attack several years later. How would this occur? Would the pathologic effects of initial cytokine upregulation remain constant? Or did they injure the CNS in such a way that future disease progression was likely? Cases alleging different injuries or theories in the Program have successfully answered these questions in connection with different injuries, like seizure disorders. *See, e.g.*, *Silverio v. Sec'y of Health & Human Servs.*, No. 15-235V, 2019 WL 6694020, at *28–30 (Fed. Cl. Spec. Mstr. Nov. 14, 2019) (varicella and pneumococcal conjugate vaccinations triggered fever in infant, which in turn caused a complex febrile seizure and subsequent epileptic seizures and disorders). But Dr. Steinman, by his admission, could not do the same here.

The fact that ADEM and MS overlap in some respects does not mean that their differences are negligible for purposes of determining entitlement herein. Indeed, their distinguishing characteristics are very important in this context. Special masters have often found that vaccines might instigate one-time, acute events in short order, such as GBS, that in turn could have significant lifelong sequelae—but which do not *themselves* progress. However, the possibility a vaccine can instigate an ever-present chronic process depends heavily on evidence that the initial harm *itself* "turns on" such a process. That evidence is lacking here, as there is little to no reliable scientific evidence filed in this case supportive of the conclusion that the first neurologic CNS injury that looks like MS will more likely than not create the conditions for a second flare—or how this would occur.

2. *Althen* Prong Three

Dr. Steinman agreed that Petitioner's INO (the presenting symptom of her alleged vaccine injury) began within twenty-four hours of receipt of the Tdap vaccine. This was entirely too short a timeframe to be medically acceptable, for several reasons.

First, the record does not suggest that proinflammatory cytokines upregulated by a vaccine could begin to cause autoimmune-mediated demyelinating injuries manifesting as INO in such a short timeframe. The fact that vaccines can initially (due to adjuvants) cause cytokines to *increase* does not also mean they become pathologic in that same time period. Dr. Steinman's say-so to the contrary was not persuasive, nor was his reliance on disparate circumstances like the short timeframe in which GBS (a peripheral neuropathy featuring acute and monophasic demyelination) might manifest post-vaccination.[22] He could not credibly demonstrate how a vaccine administered

[22] Dr. Steinman cited Schonberger for this proposition—an item of literature invoked in virtually any case where a petitioner hopes to prove a vaccine caused an autoimmune demyelinating injury. *See, e.g.*, *McKown v. Sec'y of Health & Human Servs.*, No. 15-1451V, 2019 WL 4072113, at *55 (Fed. Cl. Spec. Mstr. July 15, 2019) (discussing the

in the periphery of the body could result in a brainstem injury, manifesting initially as INO, within a day's time.

Second, Petitioner did not persuasively establish that even if the Tdap vaccine had instigated an immediate demyelinating injury sufficient to manifest as INO or ADEM, that this process would then become sufficiently chronic such that four years later a *second* flare would occur, revealing that Petitioner had MS the entire time. Dr. Steinman was particularly conclusory in setting forth this aspect of his opinion, focusing on the locus of CNS inflammation but assuming without much explanation that whatever process the vaccine started would continue to smolder in the brain for years thereafter. No persuasive showing, arising from reliable evidence, was made explaining how a single vaccination could trigger such a lengthy and persistent process. It is not enough to simply invoke the fact that vaccine injuries are rare, or that "some" unknown factor specific to a petitioner likely contributed to the situation, to make up for the absence of reliable explanatory scientific or medical evidence.

3. *Althen* Prong Two

Petitioner in this case can unquestionably point to treater support for her claim, both for her favored presenting diagnosis (ADEM) as well as the purported association of her vaccination to the injury (not to mention the temporal relationship between vaccine and initial symptoms). But I am not obligated to blindly accept treater views—and I note that the *overall* medical record preponderantly establishes her actual injury was MS, an illness far *less* associated with vaccination than one-time acute CNS demyelinating events, like ADEM or TM. That same record also unquestionably reveals that the same treaters early on recognized that Petitioner might actually have MS (corroborated by findings such as the oligoclonal band test results[23]), and in response adopted a watchful waiting treatment approach that unfortunately proved prescient. Dr. Steinman himself *agreed* that he too would have suspected MS, based on Petitioner's clinical presentation.

irrelevance of Schonberger where the alleged injury and vaccine differ from those discussed in the study). Schonberger, however, addresses only GBS, a peripheral neuropathy known to be mediated by autoantibodies, and thus reflects an aberrant *adaptive* immune response (whereas in this case Dr. Steinman's theory is that Petitioner's INO was the product *not* of an autoimmune cross-reaction, but attributable to cytokines generated in an *innate* immune response). In addition, the early-onset cases of GBS observed within one to three days of vaccination were *not* characterized by Schonberger's authors as vaccine-attributable. Schonberger at 110–12 and Figure 5. As a result, the fact that some cases of GBS began so quickly says nothing about whether Petitioner's twenty-four-hour post-vaccination onset was itself medically reasonable.

[23] Both experts also found somewhat significant the lesions observed from Petitioner's first MRI as possible proof that her disease process predated her INO symptoms (hence allowing for the inference that her MS process was subclinical at the time of vaccination). However, Drs. Steinman and Gelfand also seemed to agree with initial treater assessments that the lesions were nonspecific to Petitioner's diagnosis, and Dr. Gelfand admitted they did not explain her INO (since the lesions were *not* found on her brainstem). I accordingly do not give these particular findings significant weight in my overall analysis, other than to note that they weakly support the inference that Petitioner's MS processes could have predated vaccination.

Tr. at 84. Thus, although Petitioner was able to marshal some facts from the record on this particular prong to suggest that the Tdap vaccine "did cause" her initial INO, the weight of evidence overall does not support that conclusion.

To be clear—I do *not* find herein that Petitioner carried her *Althen* prong two burden, but rather that she offered some reliable support favoring this component of her claim, such as Dr. Sloane's opinion. The record ultimately better supports the conclusion that her presenting INO symptoms were not vaccine-caused, were not part of a post-vaccine, one-time monophasic event, and more likely reflected a disease process that could have begun prior to vaccination. There was also nothing in the record corroborating the contention that an innate immune response caused the INO symptoms, whether in the form of a test result revealing systemic inflammation elsewhere or some other symptom of cytokine reaction, like a fever.

CONCLUSION

Ms. Samuels was a highly sympathetic and credible witness, and I have no doubt she has suffered greatly with her disease. She is to be commended for her resilience in grappling with its deleterious effects, as well as in seeking an explanation for why she experienced it at all. But the evidence submitted in this case does not allow me to conclude that the Tdap vaccine could initiate a chronic disease process later resulting in MS—however the initial symptoms are defined—or that such a process could begin so close-in-time to vaccination. I therefore cannot decide entitlement in her favor.

In the absence of a timely-filed motion for review (see Appendix B to the Rules of the Court), the Clerk shall enter judgment in accord with this decision.[24]

IT IS SO ORDERED.

s/Brian H. Corcoran
Brian H. Corcoran
Chief Special Master

[24] Pursuant to Vaccine Rule 11(a), the parties may expedite entry of judgment by filing a joint notice renouncing their right to seek review.